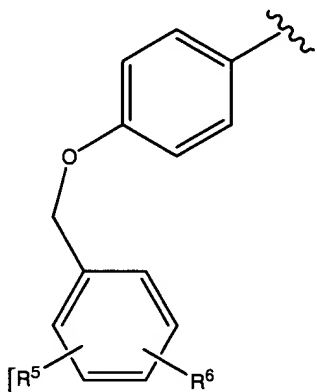


This listing of claims will replace all prior version, and listings, of claims in the application:

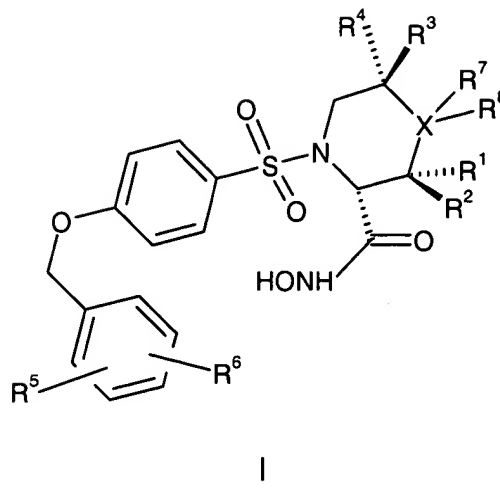
Listing of Claims:

Claims 1-15 (canceled).

16. (currently amended) A method for treating a medical condition of the type that is characterized by the destruction of articular cartilage in a human subject; wherein said medical condition comprises joint injury, reactive arthritis, acute pyrophosphate arthritis (pseudogout), psoriatic arthritis, osteoarthritis, or juvenile rheumatoid arthritis; which method comprises administering to the subject having, said condition a therapeutically effective amount of a ~~carboxylic acid hydroxamide derivative having a molecular weight of under 2000 g/mole, wherein said derivative comprises the following substituent:~~



~~wherein R⁵ and R⁶ are independent substituents in the ortho, meta, or para positions and are independently selected from the group consisting of hydrogen, halogen, cyano, methyl, and ethyl, and the carboxylic acid hydroxamide derivative exhibits an aggrecanase IC₅₀ of less than about 20 nM, said aggrecanase IC₅₀ measured by an aggrecanase chondrocyte assay~~ compound represented by formula I:



or a therapeutically acceptable salt thereof, wherein

X is carbon or nitrogen;

R¹ and R² are independently selected from the group consisting of hydrogen, hydroxy, and methyl, wherein at least one of R¹ and R² is methyl;

R³ and R⁴ are independently selected from the group consisting of hydrogen, hydroxy, and methyl, or R³ and R⁴ may be taken together to form a carbonyl group; and

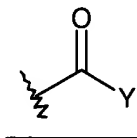
R⁵ and R⁶ are independent substituents in the ortho, meta, or para positions and are independently selected from the group consisting of hydrogen, halogen, cyano, methyl, and ethyl;

with the provisos:

when X is carbon, then R⁷ and R⁸ are both hydrogen and at least one of R¹, R², R³, and R⁴ is hydroxy;

when X is carbon and R⁵ is para-halo, then at least one of R⁶, R³, and R⁴ is not hydrogen;

when X is nitrogen, then R⁸ is not present and R⁷ is hydrogen or a group of the formula:



wherein, Y is -CH₂-NH₂ or -NH-CH₃; and

when X is nitrogen and R⁷ is H, then R³ and R⁴ are taken together to form a carbonyl group.

Claims 17-23 (Canceled).

24. (New) The method according to claim 16, wherein the medical condition is osteoarthritis.
25. (New) The method of claim 16, wherein X is carbon.
26. (New) The method of claim 25, wherein the medical condition is osteoarthritis.
27. (New) The method of claim 26, wherein the compound is selected from the group consisting of:
- (2*R*,3*R*) 1-[4-(2,4-dichloro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(2,4-dichloro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(2-chloro-4-fluoro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(2-chloro-4-fluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(2-fluoro-4-chloro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*S*) 1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,5*R*) 1-[4-(2-methyl-3-fluoro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
 - (2*R*,3*R*) 1-[4-(2-fluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;

(2*R*,3*R*) 1-[4-(2-chloro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2-methyl-3-fluorobenzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,5*R*) 1-[4-(2-methyl-5-chloro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2,4-difluoro-benzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,5*R*) 1-[4-(2-fluoro-5-chloro-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide;
(2*R*,3*R*) 1-[4-(2-methyl-5-fluorobenzyloxy)-benzenesulfonyl]-3-hydroxy-3-methyl-piperidine-2-carboxylic acid hydroxyamide; and
(2*R*,5*R*) 1-[4-(2-bromo-benzyloxy)-benzenesulfonyl]-5-hydroxy-3,3-dimethyl-piperidine-2-carboxylic acid hydroxyamide.

28. (New) The method of claim 16, wherein X is nitrogen.

29. (New) The method of claim 28, wherein the medical condition is osteoarthritis.

30. (New) The method of claim 29, wherein the compound is selected from the group consisting of:

(2*R*,3*S*) 1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-4-aminoacetyl-3-methyl-piperazine-2-carboxylic acid hydroxyamide;
(2*R*,3*S*) 1-[4-(4-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-methyl-5-oxo-piperazine-2-carboxylic acid hydroxyamide;
(2*R*,3*S*) 4-[4-(2-ethyl-benzyloxy)-benzenesulfonyl]-3-methyl-4-carboxylic acid methylamide-piperazine-2-carboxylic acid hydroxyamide;
(2*R*,3*S*) 4-[4-(5-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-3-methyl-4-carboxylic acid methylamide-piperazine-2-carboxylic acid hydroxyamide;

(2*R*,3*S*) 1-[4-(2-methyl-5-fluoro-benzyloxy)-benzenesulfonyl]-3-methyl-5-oxo-piperazine-2-carboxylic acid hydroxyamide; and

(2*R*,3*S*) 4-[4-(2,4-difluoro-benzyloxy)-benzenesulfonyl]-3-methyl-4-carboxylic acid methylamide-piperazine-2-carboxylic acid hydroxyamide.

31. (New) The method of claim 16, wherein the medical condition is psoriatic arthritis.